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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,014	LI ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,10,12-14,30,33 and 44-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5,9,10,12-14,30,33 and 44-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Non-Final Office Action is a reply to the Amendment and Response of 3 July 2003 (hereinafter, 3 July Paper) filed in response to the Non-Final Office Actin mailed 3 April 2003 (hereinafter, 3 April Office Action). Claims 5-14, 30, 33 and 44-52 were considered in the 3 April Office Action. Claims 6-8, 11, and 47-52 were cancelled and claims 5, 9, 12, 30, 33, 45 and 46 were amended in the 3 July Paper. Claims 5, 9, 10, 12-14, 30, 33 and 44-46 are presently pending and under consideration.

Response to Amendment

Rejection of claims 6-8, 11, and 47-52 is rendered moot by cancellation.

Claim Rejections - 35 USC § 112

Rejection of claims 5, 9, 10, 12-14, 30 and 33 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claimed subject matter for the reasons set forth in the 3 April Office Action is withdrawn.

Rejection of claims 30, 33, 45 and 46 under 35 U.S.C. 112, first paragraph, as lacking enablement for the reasons set forth in the 3 April Office Action is withdrawn.

Rejection of claims 5, 9, 10, 12-14, 30 and 33 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn.

Claim Rejections - 35 USC § 102

Rejection of claims 9 and 44 under 35 U.S.C. 102(b) as being clearly anticipated by NCBI online, Accession No. AC008687 (hereinafter AC008687; made of record in the IDS filed 30 August 2001) is withdrawn.

Claims 5 and 10 stand rejected and claims 12-14, 30 and 33 are newly rejected under 35 U.S.C. 102(b) as being anticipated by NCBI online, Accession No. AC008687 (hereinafter AC008687; made of record in the IDS filed 30 August 2001).

Applicant has amended claim 5 such that it is limited to an isolated nucleic acid comprising a nucleic acid sequence encoding a polypeptide comprising SEQ ID NO: 8 and has submitted an alignment demonstrating that the BAC clone sequence published in AC008687 does not comprise the contiguous sequence of SEQ ID NO: 7. However, it is clear that the portion of chromosome 19 comprised in the BAC clone is the gene encoding the polypeptide set forth as SEQ ID NO: 8. This is further evidenced by Applicant's assertion in the paragraph bridging pages 21-22 that the claimed nucleic acid is a marker for human chromosome 19. Furthermore, alignment of portions of SEQ ID NO: 7 with the AC008687 sequence indicates that AC008687 comprises the 5' coding sequence of the instant SEQ ID NO: 7 in the region of 84300 to 84100 and the 3' coding sequence of SEQ ID NO: 7 in the region of 81500 to 81300. As AC008687 appears to comprise the complete genomic sequence encoding the NOV4 protein, the skilled artisan would expect, absent evidence to the contrary, that AC008687 encodes the amino acid sequence of SEQ ID NO: 8 according to the limitations of claim 5.

Applicant has also amended claims 12-14 such that they depend directly from claim 5 and are no longer subject to the limitations of claim 11. As AC008687 is a BAC clone, it would be comprised within a vector according to claim 12 and a host cell according to claim 14. Further, the transcriptional start site of the claimed NOV4 nucleic acid is found some 84,000 base pairs from the end of the BAC clone. The skilled artisan would thus expect that the NOV4 promoter would also be comprised within the BAC clone and operably linked to the nucleic acid sequence according to claim 13.

Applicant has also amended claims 30 and 33 such that they are no longer directed to a pharmaceutical composition or kit comprising a pharmaceutical composition, but are instead directed to a composition comprising the nucleic acid of claim 5 in a pharmaceutically acceptable carrier. The specification defines "pharmaceutically acceptable carrier" as including any and all solvents (page 85, line 9-10). The skilled artisan would understand that a composition comprising the nucleic acid in a solvent would be inherent to the construction and sequencing of a BAC clone. Therefore, the BAC clone disclosed as comprising the AC008687 sequence also anticipates the limitations of claims 30 and 33.

Rejection of claims 5 and 12-14 under 35 U.S.C. 102(b) as being anticipated by Kalman *et al.* (1998) *J. Biol. Chem.* 273:5851-5857 is withdrawn.

New Grounds

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 14 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is directed to a cell comprising a vector. As the specification teaches that the host cells of the invention also include progeny or potential progeny of the cell (paragraph bridging pages 80-81) and a human being is not excluded from the potential progeny, the claimed subject matter encompasses a genetically modified human. Amending the claim such that it is directed to an "isolated host cell" would overcome this rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 9, 10, 12-14, 30, 33 and 44-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Although it was previously indicated that the specification is enabling for a nucleic acid encoding the polypeptide set forth as SEQ ID NO: 8, upon further consideration it is clear that the specification fails to teach the skilled artisan how to use the nucleic acid for the specific and substantial credible utilities set forth in the specification without undue experimentation.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims: The claims are directed to a nucleic acid molecule encoding the human polypeptide set forth as SEQ ID NO: 8 (*Id.*), which has significant structural homology with a family of voltage gated potassium channels. The specification asserts that the nucleic acid is useful as a marker for human chromosome 19 and for therapeutic application in Episodic Ataxia, type 1, Long QT Syndrome 1 and 2, Benign Neonatal Epilepsy, Jervell and Lange-Neilson syndrome, Autosomal dominant deafness (DFNA 2), non-insulin dependent diabetes mellitus, CNS disorders, arrhythmia, seizure, asthma, hypertension therapy and/or other pathologies and disorders. The specification further asserts that the nucleic acid can be used for identification of therapeutics which modulate the channel and therefore modulate insulin secretion. The enabling specification must therefore teach the skilled artisan how to use the claimed nucleic acid for these purposes without having to engage in undue experimentation.

State of the prior art and level of predictability in the art: First, although the art teaches a nucleic acid encoding a polypeptide comprising the instant SEQ ID NO: 8, the art is silent with

regard to the function of the polypeptide or how to use the polypeptide. The art does teach that the voltage gated potassium channel family is functionally diverse and there is no utility that is common to all members of the family. Christie *et al.* (1995) *Clin. Exp. Pharmacol. Physiol.* 22:944-951 teaches that Kv channels in mammals are structurally and functionally diverse and are differentially distributed among different cell groups (see especially the section entitled "Structural diversity of Kv channels in mammals" beginning on page 946, and the paragraph bridging pages 948-949). Wickenden (2002) *Pharmacol. Ther.* 94:157-182, in discussing the state of the art with regard to potassium channels as therapeutic drug targets, teaches that the physiological role of potassium channels in pathologies is extraordinarily complex and unpredictable. In particular Wickenden teaches that different tissues contain different complements of potassium channels which may or may not contribute to a disease sate or therapeutic intervention. For example, Wickenden teaches, *inter alia*, that Kv1.3 channels are found in lymphocytes and contribute to lymphocyte activation (section 6.1.1), that there are a several different types of potassium channels found in cardiac cells some of which may contribute to long QT syndrome (e.g., h-ERG (section 6.2.1) or KCNQ1 and KCNE1 (section 6.2.2)) and some of which may be targets for treatment of atrial fibrillation (e.g., Kv1.5 (section 6.2.5)), that altered distribution of Kv1.1 and Kv1.2 may be responsible for axonal dysfunction in conditions associated with demyelination (see section 6.3), that CNS neurons are endowed with many kinetically and pharmacologically distinct potassium currents (see section 6.4), that Kv4.2 may enhance synaptic plasticity (see section 6.4.4), that Kv1.1 may be involved in partial seizures in humans (see section 6.4.4) and that the channel primarily responsible for insulin secretion from pancreatic β-cells is I_{KATP} (see section 6.4.4). Finally, Wickenden teaches, "a

combination of biophysical, pharmacological, and genetic approaches has started to provide an understanding of the molecular composition of many important native K^+ channels ...Much work remains to be done, however, before the full potential of K^+ channel modulators can be realized. It will be particularly important in the post-genome era to understand what role each K^+ channel gene product plays in the formation of native currents and what role each molecularly defined K^+ current plays in cellular physiology and pathophysiology" (paragraph bridging the left and right columns on page 171).

Viewed as a whole, the teachings from the relevant art indicate that polypeptides having the structure of a voltage gated potassium channel could play a role in any one of a variety of physiological or pathological conditions and that, given the state of the art even as of 2002 (when Wickenden was published), one of ordinary skill would not know what the physiological or pathological function of a polypeptide would be based only on its structural similarity to the family of voltage gated potassium channels. Therefore, based on the teachings of the art, the skilled artisan would not know what conditions within the unlimited list contemplated in the specification might be amenable to treatment or diagnosis according to the teachings of the specification. Thus, the skilled artisan is dependent upon the teachings of the disclosure to provide specific guidance as to how to use the claimed nucleic acid for the purposes set forth therein.

Amount of direction provided by the inventor and existence of working examples: The specification (beginning at page 16 and continued through page 21) teaches that the polypeptide having the sequence of SEQ ID NO: 8 shares significant homology with a family of voltage-gated potassium channels and thus would credibly have the function of a voltage-gated

potassium channel. The specification teaches that nucleic acids encoding the polypeptide set forth as SEQ ID NO: 8 can be used to produce the protein, to raise antibodies, to detect mRNA, to detect genetic lesions, to modulate activity of the protein and to screen for drugs or compounds. However, the specification fails to teach to what purpose the nucleic acid, or protein and antibodies produced therefrom, will be applied. The specification suggests that the claimed nucleic acid can be used as marker for chromosome 19; however, this is not a patentable utility because it is not specific to the claimed nucleic acid. With regard to treatment or diagnosis of one of the multitude of diseases contemplated in the specification, the disclosure provides no teaching that would indicate that the NOV4 protein or nucleic acid could be used as a therapeutic reagent, or is a target for therapeutic target in any of those diseases.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention: Although the relative level of skill in the art is high, the skilled artisan would not be able to use the claimed invention without first engaging in undue experimentation. The asserted utilities for the claimed nucleic acid appear to be based on its encoding a polypeptide that is likely a voltage gated potassium channel and physiological functions established for other members of the family. However, the art teaches that there are many different proteins belonging to the family of voltage gated potassium channels. These proteins are expressed in different tissues and are involved in various physiological and pathophysiological processes. Given this functional diversity, the skilled artisan would be unable to use the claimed nucleic acid, or other reagents developed therefrom, for the specific and substantial credible utilities asserted in the specification without first engaging in empirical experimentation to establish a nexus between the functioning of the NOV4 protein and some physiological or pathological state. In other

words, based on the structure of the NOV4 protein the skilled artisan would know that the protein can conduct a potassium current, but would not know how to use a nucleic acid encoding such a protein without engaging in undue experimentation to establish what role that potassium current played in the functioning of an organism. With regard to therapeutic uses for the claimed invention, the specification provides no specific guidance as to how the claimed nucleic acids or agents developed therewith can be used therapeutically. All of the teachings in the specification related to therapy are general in nature and based on circumstantial evidence. Therefore, the skilled artisan seeking to use the claimed invention therapeutically or in the identification or production of therapeutics would have to engage in undue experimentation to first identify a disease that could be treated, develop an effective therapeutic agent and then develop an effective treatment regimen. This degree of experimentation is clearly beyond what is considered routine in the art. Therefore, the skilled artisan would not be able to use the claimed invention without undue experimentation.

Thus, due to the art recognized unpredictability of the physiological or pathophysiological significance of any given voltage gated potassium channel and the lack of guidance in the specification or prior art with regard to how to use the claimed nucleic acid for the specific and substantial credible utilities set forth in the specification, it would require undue experimentation to use the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Please note: Art Unit 1636 will be moving to the new USPTO facilities on 14 January 2004. After that date, Examiner Sullivan can be reached at 571-272-0779 and Examiner Yucel can be reached at 571-272-0781.

Anne-marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

DMS